

REMARKS

Claim 2 has been amended to recite that the microorganism is "*Xanthophyllomyces dendrorhous* (*Phaffia rhodozyma*) ATCC96594, redeposited under accession No. ATCC 74438". Support for the amendment is found in the specification¹ at, for example, paragraphs 4, 5, 7, Example 1 (paragraph 24, line 1), and Example 2 (paragraph 27, line 1); and in original claim 3. *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

Claim 2 has also been amended to replace the phrase "an inhibitor of biosynthesis of sterols from farnesyl pyrophosphate" with "[3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine". Support for the amendment is found in the specification at, for example, paragraph 13, lines 1-7, paragraph 14, lines 1-3, paragraph 23, lines 1-3, Example 1 (paragraph 24, lines 6-7), and Example 2 (paragraph 27, lines 5-6); and original claims 16 and 17. (Id.)

In addition, claim 2 has been amended to delete the recitation with regard to the concentration of the inhibitor in an aqueous medium of "within a range that gives less than a 50 % reduction of cell growth as compared to cell growth in the absence of the inhibitor under carotenoids-producing conditions and cell growth is determined by measuring the optical density of a sample of the cultured medium at 660 nm", and to replace it with "from 0.5 µg/ml to 5.0 µg/ml". Support for the amendment is found in the

¹ References to the specification identify portions of the published application, US2005/0260700.

specification at, for example, Example 1 (Table 1 and paragraph 26) and Example 2 (Table 2 and paragraph 30).

Claim 2 has also been amended to delete the recitation, "wherein the astaxanthin content of the isolated carotenoids is greater than that which results from cultivating in the absence of an inhibitor of biosynthesis of sterols from farnesyl pyrophosphate".

Claims 1, 3-19, and 22-24 have been canceled, without prejudice.

No new matter has been added.

Claims 2, 20, and 21 are pending.

Interview Summary

The undersigned thanks Examiner Irene Marx for the courtesies extended during the telephonic Interview which was held on June 24, 2009. As noted in the Examiner's Interview Summary (Paper No. 20090624), the Examiner made recommendations regarding the claim language, and potential amendments were discussed. The data disclosed in Tables 1 and 2 of the specification was also discussed. Further information regarding the telephonic Interview is noted within subsequent remarks.

Indefiniteness Rejections

Claims 2-3, 13, and 15-24 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. (Paper No. 20090213 at 2.)

In making the rejection, the Examiner asserted that "[c]laim 2 is vague, indefinite and confusing in the recitation of 'greater than'." (Id.) The Examiner further asserted that "the specification does not enable one skilled in the art to reasonably establish what may be construed as being within the metes and bounds of the limitation as modified by the word of degree. Therefore, one of ordinary skill in the art would not be apprised as to the claimed invention's scope when the claims are read in light of the specification." (Id.)

The Examiner also contended that "[c]laim 2 is confusing in that applicant fails to set forth the criteria that define a 'concentration of the said inhibitor' other than providing a functional definition of 'inhibitor' as 'giving less than ... reduction of the cell growth' of undefined microorganisms using undefined inhibitors. Also, it is unclear how the concentration correlates with the production of 'greater' astaxanthin content...". (Id. at 2-3.) The Examiner further asserted that "[s]uch functional language describes nothing about the chemical, physical or structural properties of the strain used, the compounds used or their concentration." (Id. at 3.)

The Examiner further asserted that certain "guidance" provided by the specification concerning a range of concentration that gives less than 50% reduction of cell growth "is not deemed to be informative as to the specific concentrations required." (Id.)

The Examiner has noted that "as to the example [disclosed in the specification], it pertains specifically to the combination of culturing *Phaffia rhodozyma* ATCC 96594 using the inhibitor [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropylamine in

various specific concentrations. This disclosure pertains to the elected species of inhibitor..." (Id. at 4.)

To forward prosecution in the present application, claim 2 has been amended to recite "[a] biological process for producing carotenoids including astaxanthin, the process comprising cultivating a microorganism which is *Xanthophyllomyces dendrorhous* (*Phaffia rhodozyma*) ATCC96594, redeposited under accession No. ATCC 74438, in the presence of [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine, a substrate for producing carotenoids which include astaxanthin, in an aqueous nutrient medium under aerobic conditions wherein the concentration of the inhibitor in the aqueous medium is from 0.5 µg/ml to 5.0 µg/ml, and isolating the resulting carotenoids which include astaxanthin, from the cells of said microorganism or from the cultured medium."

It is submitted that the amendments reciting the strain of microorganism and inhibitor in amended claim 2 are sufficient under 35 U.S.C § 112, second paragraph. The Examiner appears to concede in the quoted portion of the Action above that one skilled in the art would understand the claim, as amended, in view of "the example" which discloses the use of the recited strain and elected inhibitor. (Id.) In addition, during the telephonic Interview, the Examiner indicated the above-identified amendments would be sufficient to overcome the rejection.

It is also submitted that the amendment reciting that the concentration of the inhibitor in the aqueous medium is "from 0.5 µg/ml to 5.0 µg/ml" is sufficient under 35 U.S.C. 112, second paragraph. During the telephonic Interview, the (now former) recitation in the claim regarding "the concentration of the inhibitor ... that gives less than

a 50 % reduction of cell growth ..." was discussed in relation to the specification. Upon discussing both Examples 1, Table 1, and Example 2, Table 2, of the specification, the Examiner agreed that an amendment reciting the concentration range "from 0.5 µg/ml to 5.0 µg/ml" would be acceptable.

In addition, functional language regarding the astaxanthin content has been deleted by amendment to claim 2.

The Examiner signaled during the Interview that all of the amendments here made to claim 2 would overcome the asserted indefiniteness of the claim.

In view of the foregoing, it is respectfully submitted that the amendment has been rendered moot. Reconsideration and withdrawal of the rejection are requested.

Obviousness Rejection

Claims 2-3, 13, and 15-24 were rejected under 35 U.S.C. § 103(a) as being unpatentable over An *et al.*, Applied and Environmental Microbiology, Jan. 1989, Vol. 51, p. 116-124 ("An") "taken with" Brown *et al.*, Phenoxypropylamines: A New Series of Squalene Synthase Inhibitors, J. Med. Chem., 1995, Vol. 38, no. 21, p. 4157-4160 ("Brown"). (Id. at 5.) In making the rejection, the Examiner asserted that "the reasons [for the rejection are] as stated in the last Office action and the further reasons [provided]." (Id.)

Both An and Brown have been summarized on the record.

The Examiner's rejection has also been summarized on the record.

In the Response to Arguments section of the Action, the Examiner acknowledged, "That the instant specification shows good overproduction of astaxanthin is not disputed." (Id. at 8.)

The Examiner asserted, *inter alia*, however, that "there is no clear correlation between the results shown and the invention as claimed, which requires minimal concentrations of inhibitors and minimal increases in carotenoid production. The touted Example 2 specifically pertains to *Phaffia rhodozyma* ATCC 96594 cultured under specific process conditions and using 0, 0.5, 1.0, 2.0, and 5.0 µg/mL, respectively, of [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine." (Id.)

The Examiner also asserted that "the results of Table 2 of the as-filed specification show that at day 4 of cultivation the results are better without addition of the specific squalene synthase inhibitor [3(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine than with the addition of 5µg/ml even for the specific strain ATCC 96584 in a specific medium. Thus, it is apparent that the length of cultivation as well as the specific concentration of the specific inhibitor [3-(3-allyl-biphenyl-4yloxy)-propyl]-isopropyl-amine affect the astaxanthin content obtained for a specific high producing strain such as *Xanthophyllomyces(Phaffia)* ATCC 96584. Yet only in dependent claim 3 is this specific strain of *Xanthophyllomyces(Phaffia)* cultured. Thus, the results presented in the specification cannot be readily extrapolated to the broad invention as claimed, since the results obtained suggest to one of ordinary skill in the art that the effects on carotenoid and astaxanthin production are dependent on the strain of *Xanthophyllomyces(Phaffia)* cultured as well as the type and concentration of inhibitor used in the culturing process." (Id.)

The Examiner concluded that "[a]ny unexpected results shown in the present written disclosure are closely tied to the strain cultured, the specific inhibitor used and the concentration of this specific inhibitor." (Id.)

To forward prosecution in the present application, claim 2 has been amended to recite "[a] A biological process for producing carotenoids including astaxanthin, the process comprising cultivating a microorganism which is *Xanthophyllomyces dendrorhous* (*Phaffia rhodozyma*) ATCC96594, redeposited under accession No. ATCC 74438, in the presence of [3-(3-allyl-biphenyl-4-yloxy)-propyl]-isopropyl-amine, a substrate for producing carotenoids which include astaxanthin, in an aqueous nutrient medium under aerobic conditions wherein the concentration of the inhibitor in the aqueous medium is from 0.5 µg/ml to 5.0 µg/ml, and isolating the resulting carotenoids which include astaxanthin, from the cells of said microorganism or from the cultured medium."

It is respectfully submitted that amended claim 2 recites the disclosed strain cultured, the specific inhibitor used in accordance with the Examples, and a concentration range of the specific inhibitor, which are correlated with the unexpected results shown in the specification. It is also noted that during the telephonic Interview, the Examiner indicated that the presently recited inhibitor concentration of "from 0.5 µg/ml to 5.0 µg/ml" is sufficiently correlated with the unexpected, beneficial results as disclosed in Example 2, Table 2, when considered in connection with the amendments reciting the strain cultured and the specific inhibitor.

In view of the foregoing, it is respectfully submitted that the rejection has been rendered moot. Reconsideration and withdrawal of the rejection are requested.

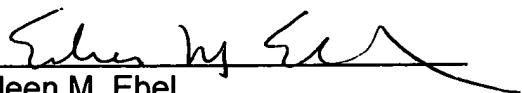
Application No.: 10/518,530
Response Dated: March 9, 2009
Reply to Office Action Dated: July 30, 2009

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the rejections and allowance of the claims are respectfully requested. If the Examiner has any questions about this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to Mail Stop Amendment, Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 30, 2009.


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